SUPPORTING INFORMATION

Title: From Acyclic to Cyclic α-Amino Vinylphosphonates by Using Ring-Closing Metathesis
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EXPERIMENTAL SECTION

GENERAL METHODS

All reactions were carried out under argon with magnetic stirring. All solvents and chemicals were purified based on standard procedures. Reagent grade solvents were used without purification for all extractions and work-up procedures. \( R_f \) values refer to values obtained by TLC on 0.25 mm silica gel plates (60F254). Flash chromatography was carried out on silica gel 60 (15–40 μm) with various mixtures of ethyl acetate (EtOAc) and petroleum ether (PE), yields refer to chromatographically and spectrosopically pure compounds. NMR spectra were recorded at 250, 300, 360, 400, 500 MHz. HRMS spectra were recorded with a MicroTOFq spectrometer.

GENERAL PROCEDURE A FOR THE PREPARATION OF THE YNAMIDES FROM THE SULFONAMIDES

Sulfonamide (2.05 mmol), CuSO\(_4\)·5H\(_2\)O (0.205 mmol), 1,10-phenanthroline (0.411 mmol), and K\(_3\)PO\(_4\) (4.11 mmol) were heated to 70 °C in 2 mL of dry toluene under inert atmosphere. Bromoalkyne (2.71 mmol) in 2 mL of dry toluene was then slowly added. After 4 h at 70 °C, the mixture was cooled to room temperature, filtered through a pad of Celite, and concentrated in vacuo. Purification by flash chromatography on silica gel yielded the ynamide.

GENERAL PROCEDURE B FOR THE PREPARATION OF THE \( \alpha \)-AAPs FROM THE YNAMIDES

To a solution of ynamide (2.05 mmol) in 16 mL of anhydrous tetrahydrofuran cooled at 0 °C were added triethylamine (2.26 mmol) and chlorophosphite (2.26 mmol). After 18 h of stirring at room temperature, the mixture was filtered through a pad of Celite\(^\circledR\), the solvent was removed in vacuo, and crude product was purified by flash chromatography on silica gel to yield the amino allenylphosphonates.


Diethyl (1-(N-(4-methoxybenzyl)methylsulfonamido)propa-1,2-dien-1-yl)phosphonate (SI01)

Prepared according to the general procedures A and B. Flash Chromatography: EtOAc/PE 20/80 to 100/0; yellow oil, 1.760 g, 49% yield; \( R_f = 0.37 \) (EtOAc); \(^1\)H NMR (250 MHz, CDCl\(_3\)) \( \delta \) 7.30 (d, \( J = 8.7 \) Hz, 2H), 6.85 (d, \( J = 8.7 \) Hz, 2H), 5.13 (d, \( J = 10.4 \) Hz, 2H), 4.64 (s, 2H), 4.20 – 4.00 (m, 4H), 3.79 (s, 3H), 3.00 (s, 3H), 1.36 – 1.27 (m, 6H); \(^13\)C NMR (62.9 MHz, CDCl\(_3\)) \( \delta \) 215.9 (d, \( J = 26.5 \) Hz), 159.3, 130.4, 127.7, 113.6, 98.1 (d, \( J = 228.4 \) Hz), 81.6 (d, \( J = 11.7 \) Hz), 63.1 (d, \( J = 6.2 \) Hz), 55.1, 52.6, 40.5, 16.1 (d, \( J = 6.6 \) Hz); \(^31\)P NMR (101.25 MHz, CDCl\(_3\)) \( \delta \) 10.1; HRMS (ESI) m/z [MH\(^+\)] calced for C\(_{16}\)H\(_{25}\)NO\(_6\)PS: 390.1135, found: 390.1135.

Dimethyl (1-((N-(4-methoxybenzyl)-4-methylphenyl)sulfonamido)-3-methylbuta-1,2-dien-1-yl)phosphonate (SI02)

I
Prepared according to the general procedures A and B. Flash Chromatography: EtOAc/PE 20/80 to 100/0; yellow solid, 2.146 g, 65% yield; \( R_f = 0.15 \) (EtOAc/PE = 60/40); mp = 105-110 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.82 (d, \( J = 8.2 \) Hz, 2H), 7.31 (d, \( J = 8.3 \) Hz, 2H), 7.23 (d, \( J = 8.6 \) Hz, 2H), 6.81 (d, \( J = 8.6 \) Hz, 2H), 4.51 (s, 2H), 3.77 (s, 3H), 3.55 (d, \( J = 11.1 \) Hz, 6H), 2.43 (s, 3H), 1.57 (d, \( J = 4.6 \) Hz, 6H); \(^1\)C NMR (62.9 MHz, CDCl\(_3\)) \( \delta \) 210.8 (d, \( J = 25.8 \) Hz), 159.1, 143.4, 136.5, 130.2, 129.4, 127.9, 113.6, 105.0 (d, \( J = 12.2 \) Hz), 94.4 (d, \( J = 237.5 \) Hz), 55.2, 53.0 (d, \( J = 6.1 \) Hz), 52.5, 21.5, 19.2 (d, \( J = 4.8 \) Hz); \(^{31}\)P NMR (101.25 MHz, CDCl\(_3\)) \( \delta \) 14.6; HRMS (ESI) m/z [MH\(^+\)] calcd for C\(_{22}\)H\(_{20}\)NO\(_6\)PS: 466.1448, found: 466.1447.
GENERAL PROCEDURE C FOR THE REDUCTION OF α-AAPs INTO α-AVPs

Quinoline (1.5 mmol) and palladium on charcoal (10wt.%; 100 mg) were added to a solution of α-AAP (1.5 mmol) in absolute ethanol (15 mL). The mixture was degassed with hydrogen, and then it was left under a hydrogen atmosphere (balloon) at room temperature for the specified reaction time (20 min to 18 h). After this time, the mixture was filtered through a pad of Celite®, and the solvent was removed from the filtrate in vacuo. The crude product was purified by flash chromatography on silica gel to give the α-AVP.


Diethyl (1-((N-(4-methoxybenzyl)-4-methylphenyl)sulfonamido)prop-1-en-1-yl)phosphonate (SI03)

Prepared according to the general procedure C. Flash Chromatography: EtOAc/PE 10/90 to 90/10; yellow oil, 1.98 g, 50% yield; Rf = 0.55 (EtOAc/PE = 80/20); Z stereoisomer: 1H NMR (250 MHz, CDCl3) δ 7.81 (d, J = 8.2 Hz, 2H), 7.25 – 7.19 (m, 2H), 7.13 – 7.05 (m, 2H), 6.76 – 6.67 (m, 2H), 5.94 (dt, J = 38.2, 8.3 Hz, 1H), 4.46 (br. s, 2H), 4.06 – 3.79 (m, 4H), 3.69 (s, 3H); 13C NMR (62.9 MHz, CDCl3) δ 159.3, 151.8 (d, J = 27.1 Hz), 143.4, 137.6, 131.4, 130.8, 129.4, 128.2, 127.7, 126.1, 113.7, 61.9 (d, J = 5.8 Hz), 55.3, 53.2, 21.6, 16.4 (d, J = 6.3 Hz), 15.3; 31P NMR (101.25 MHz, CDCl3) δ 12.1; Characteristic signals for E isomer: 1H NMR (250 MHz, CDCl3) δ 7.90 (d, J = 8.3 Hz, 2H), 6.90 – 6.79 (m, 1H), 4.62 (d, J = 14.3 Hz, 1H), 4.26 (s, J = 14.3 Hz, 1H), 2.42 (s, 3H), 1.45 (dd, J = 6.9, 3.0 Hz, 3H); 13C NMR (62.9 MHz, CDCl3) δ 159.5, 151.2, 113.6, 52.3; 31P NMR (101.25 MHz, CDCl3) δ 13.9; HRMS (ESI) m/z [MNa+] calcd for C22H30NNaO6PS: 490.1424, found: 490.1411.

Diethyl (1-((N-(4-methoxybenzyl)-4-methylphenyl)sulfonamido)but-1-en-1-yl)phosphonate (SI04)

Prepared according to the general procedure C. Flash Chromatography: EtOAc/PE 30/70 to 70/30; yellow oil, 331 mg, quantitative yield; Rf = 0.60 (EtOAc/PE = 80/20); IR (neat) 2978, 2932, 2870, 1736, 1613, 1512, 1451 cm⁻¹; Z stereoisomer: 1H NMR (400 MHz, CDCl3) δ 7.75 (d, J = 8.2 Hz, 2H), 7.25 – 7.19 (m, 2H), 7.13 – 7.05 (m, 2H), 6.76 – 6.67 (m, 2H), 5.94 (dt, J = 38.2, 8.3 Hz, 1H), 4.46 (br. s, 2H), 4.06 – 3.79 (m, 4H), 3.69 (s, 3H), 2.35 (s, 3H), 2.31 – 2.22 (m, 2H), 1.17 (t, J = 7.1 Hz, 6H), 0.77 (t, J = 7.5 Hz, 3H); 13C NMR (126 MHz, CDCl3) δ 159.3, 158.1 (d, J = 28.0 Hz), 143.4, 137.4, 131.0, 129.4, 128.2, 127.9, 126.2 (d, J = 212.0 Hz), 113.6, 61.9 (d, J = 5.9 Hz), 55.3, 53.2, 22.6 (d, J = 2.7 Hz), 21.6, 16.4 (d, J = 6.6 Hz), 12.8 (d, J = 1.8 Hz); 31P NMR (162 MHz, CDCl3) δ 12.3; Characteristic signals for E isomer: 1H NMR (400 MHz, CDCl3) δ 7.83 (d, J = 8.3 Hz, 2H), 6.67 – 6.54 (m, 1H), 4.37 (dd, J = 138.9, 14.3 Hz, 2H), 2.36 (s, 3H), 0.54 (t, J = 7.5 Hz, 3H); 13C NMR (126 MHz, CDCl3) δ 159.4, 157.8 (d, J = 26.8 Hz), 137.7, 131.4, 129.4, 128.0, 127.6, 124.8 (d, J = 213.7 Hz), 113.6, 62.1 (d, J = 6.4 Hz), 52.1, 12.1; 31P NMR (162 MHz, CDCl3) δ 14.2; HRMS (ESI) m/z [MNa+] calcd for C23H32NNaO6PS: 504.1580, found: 504.1560.

Diethyl (1-((N-(4-methoxybenzyl)methylsulfonamido)prop-1-en-1-yl)phosphonate (SI05)

Prepared according to the general procedure C. Flash Chromatography: EtOAc/PE 20/80 to 80/20; orange oil, 354 mg, 80% yield; Rf = 0.37 (EtOAc/PE = 90/10); Z stereoisomer: 1H NMR (300 MHz, CDCl3) δ 7.26 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 6.22 (dq, J = 37.6, 7.6 Hz, 1H), 4.55 (s, 2H), 4.21 – 4.06 (m, 4H), 3.79 (s, 3H), 3.12 (s, 3H), 1.87 (dd, J = 7.6, 3.1 Hz, 3H), 1.34 (t, J = 7.1 Hz, 6H); 13C NMR (75 MHz, CDCl3) δ 159.0, 153.0 (d, J = 28.1 Hz), 130.2, 127.9, 126.3 (d, J = 170.0 Hz), 113.5, 61.8 (d, J = 5.6 Hz), 54.9, 52.5, 39.6, 16.0 (d, J = 6.5 Hz); 31P NMR (121.5 MHz, CDCl3) δ 13.3; Characteristic signals for E isomer: 1H NMR (300 MHz, CDCl3) δ 7.33 (d, J = 8.7 Hz, 2H), 6.81 – 6.68 (m, 1H), 4.81 – 4.31 (m, 2H), 3.78 (s, 3H), 3.11 (s, 3H), 1.41 (dd, J = 6.9, 3.1 Hz, 3H);
C NMR (75 MHz, CDCl₃) δ 159.2, 150.8 (d, J = 28.4 Hz), 130.9, 113.3, 62.1 (d, J = 5.8 Hz), 52.0, 39.5, 14.7; ¹³P NMR (121.5 MHz, CDCl₃) δ 14.1; HRMS (ESI) m/z [MNa⁺] calcd for C₁₆H₂₆NNaO₆PS: 414.1111, found: 414.1108.

Dimethyl (1-(N-(4-methoxybenzyl)-4-methylphenyl)sulfonamido)-3-methylbut-1-en-1-yl)phosphonate (SI06)

Prepared according to the general procedure C. Flash Chromatography: EtOAc/PE 70/30; colorless oil, 192 mg, 81% yield; Rₜ = 0.63 (EtOAc); Z stereoisomer ¹H NMR (300 MHz, CDCl₃) δ 7.81 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 7.17 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 5.75 (dd, J = 38.8, 11.4 Hz, 2H), 4.52 (br. s, 1H), 3.78 (s, 3H), 3.62 (d, J = 11.2 Hz, 6H), 3.12 – 2.94 (m, 1H), 2.45 (s, 3H), 0.83 (br. s, 6H); ¹³C NMR (91 MHz, CDCl₃) δ 163.1 (d, J = 28.7 Hz), 159.2, 143.3, 137.0, 131.0, 129.3, 127.9 (d, J = 7.4 Hz), 127.5, 123.6 (d, J = 214.1 Hz), 113.5, 55.2, 53.1, 52.4, 28.3, 21.5 (d, J = 5.5 Hz); ³¹P NMR (121.25 MHz, CDCl₃) δ 15.3; Characteristic signals for E isomer: ¹H NMR (300 MHz, CDCl₃) δ 7.89 (d, J = 8.3 Hz, 2H), 6.48 (dd, J = 12.8, 10.9 Hz, 1H), 4.67 (d, J = 14.4 Hz, 1H), 4.23 (dd, J = 14.4, 1.6 Hz, 1H), 3.66 (d, J = 11.1 Hz, 6H), 1.05 (d, J = 6.5 Hz, 3H), 0.24 (d, J = 6.5 Hz, 3H); ¹³C NMR (91 MHz, CDCl₃) δ 162.6 (d, J = 25.8 Hz), 159.4, 137.4, 131.2, 123.0, 127.9, 121.5 (d, J = 212.1 Hz), 113.7, 28.8; ³¹P NMR (121.25 MHz, CDCl₃) δ 17.2; HRMS (ESI) m/z [MH⁺] calcd for C₂₂H₃₁NO₆PS: 468.1579, found: 468.1604.
$^{1}H$ AND $^{13}C$ NMR SPECTRA

Spectra of the $\alpha$-AAPs 13
**$^1$H NMR – 250 MHz – CDCl$_3$**

![$^1$H NMR spectrum](image)

**$^{13}$C NMR – 62.9 MHz – CDCl$_3$**

![$^{13}$C NMR spectrum](image)
**$^{1}$H NMR – 250 MHz – CDCl$_3$**

- Peaks at 7.84, 7.81, 7.32, 7.29, 7.25, 7.26, 7.29, 7.32, 5.09, 2.08, 2.14, 2.15, 3.06, 3.53, 3.57, 3.77, 4.51, 6.79, 6.82, 7.22, 7.25, 7.26, 7.29, 7.32.

**$^{13}$C NMR – 62.9 MHz – CDCl$_3$**

SPECTRA OF THE PMB-PROTECTED α-AVPs 14
**$^1H$ NMR – 250 MHz – CDCl$_3$**

![1H NMR spectrum](image)

**$^{13}C$ NMR – 62.9 MHz – CDCl$_3$**

![13C NMR spectrum](image)
**$\text{^1H NMR – 300 MHz – CDCl}_3$**

![H NMR spectrum](image)

**$\text{^13C NMR – 75 MHz – CDCl}_3$**

![C NMR spectrum](image)
Spectra of the deprotected α-AVPs 15
» **\(^1\)H NMR – 250 MHz – CDCl\(_3\)**

![H NMR spectrum](image)

\((E)-15a\)

» **\(^1\)C NMR – 62.9 MHz – CDCl\(_3\)**

![C NMR spectrum](image)
$^1$H NMR – 250 MHz – CDCl$_3$

![1H NMR spectrum](image)

$^{13}$C NMR – 62.9 MHz – CDCl$_3$

![13C NMR spectrum](image)
\[ \text{1H NMR – 300 MHz – CDCl}_3 \]

\[ \text{13C NMR – 62.9 MHz – CDCl}_3 \]
» **1H NMR – 250 MHz – CDCl₃**

![1H NMR spectrum with peaks at various ppm]

(Z)-15c

» **13C NMR – 62.9 MHz – CDCl₃**

![13C NMR spectrum with peaks at various ppm]

[(Z)-15c](P(OEt)₂)N(Ts)(i-Pr)
$^1$H NMR – 300 MHz – CDCl$_3$

$^{13}$C NMR – 75 MHz – CDCl$_3$

(Z)-15d
» **¹H NMR – 500 MHz – CDCl₃**

![¹H NMR spectrum](image)

(Z)-15e

» **¹³C NMR – 126 MHz – CDCl₃**

![¹³C NMR spectrum](image)
SPECTRA OF THE $\alpha$-AVPs 16
**1H NMR – 400 MHz – CDCl₃**

![1H NMR spectrum](image)

**13C NMR – 101 MHz – CDCl₃**

![13C NMR spectrum](image)
**$^1$H NMR – 360 MHz – CDCl$_3$**

![NMR spectrum](image)

**$^{13}$C NMR – 91 MHz – CDCl$_3$**

![NMR spectrum](image)
**$^1$H NMR – 400 MHz – CDCl$_3$**

![$^1$H NMR spectrum](image)

**$^{13}$C NMR – 126 MHz – CDCl$_3$**

![$^{13}$C NMR spectrum](image)
1H NMR – 400 MHz – CDCl₃

13C NMR – 126 MHz – CDCl₃
\[ {^1}\text{H NMR} - 500\text{ MHz} - \text{CDCl}_3 \]

\[ {^{13}\text{C NMR} - 126\text{ MHz} - \text{CDCl}_3} \]

\[ 16e \]

\[ \text{Ms} \quad \text{O} \quad \text{OEt} \]

\[ \text{N} \quad \text{OEt} \quad \text{Me} \]
$^1$H NMR – 300 MHz – CDCl$_3$  

$^{13}$C NMR – 91 MHz – CDCl$_3$
**$^1$H NMR – 400 MHz – CDCl$_3$**

![1H NMR spectrum](image)

**$^{13}$C NMR – 126 MHz – CDCl$_3$**

![$^{13}$C NMR spectrum](image)
$$^{1}$$H NMR – 500 MHz – CDCl$_3$

![NMR spectrum of 16h](image)

$$^{13}$$C NMR – 126 MHz – CDCl$_3$

![C NMR spectrum of 16h](image)
$$^1$$H NMR – 400 MHz – CDCl$_3$

$$^{13}$$C NMR – 126 MHz – CDCl$_3$
**1H NMR – 400 MHz – CDCl₃**

![1H NMR spectrum for compound 16k]

- ν (ppm): 7.26, 7.27, 7.29, 7.60, 7.92, 5.93, 5.96, 5.98, 2.10, 2.14, 2.17, 2.20, 2.18, 2.19, 2.41, 3.12, 3.13, 3.15, 3.16, 3.18, 3.19, 3.21, 3.43, 3.45, 3.47, 3.70, 3.73

**13C NMR – 126 MHz – CDCl₃**

![13C NMR spectrum for compound 16k]


**Molecular Structure**

- Ts
- N
- P
- OMe
- OMe
- i-Pr
» **H NMR – 300 MHz – CDCl₃**

![H NMR spectrum]

» **C NMR – 91 MHz – CDCl₃**

![C NMR spectrum]
» $^1$H NMR – 250 MHz – CDCl$_3$

» $^{13}$C NMR – 62.9 MHz – CDCl$_3$
« ¹H NMR – 250 MHz – CDCl₃

16n

¹³C NMR – 62.9 MHz – CDCl₃
**$^1$H NMR – 360 MHz – CDCl$_3$**

![NMR Spectrum](image)

**$^{13}$C NMR – 91 MHz – CDCl$_3$**

![C NMR Spectrum](image)
**$^1$H NMR – 250 MHz – CDCl$_3$**

![H NMR spectrum](image)

**$^{13}$C NMR – 62.9 MHz – CDCl$_3$**

![C NMR spectrum](image)
SPECTRA OF THE PRODUCTS OF METATHESIS
™ 1H NMR – 400 MHz – CDCl₃

![1H NMR spectrum](image)

™ 13C NMR – 91 MHz – CDCl₃

![13C NMR spectrum](image)
1H NMR – 400 MHz – CDCl$_3$

$\text{OEt}$

$\text{OEt}$

$\text{Ms}$

17b

$\text{13C NMR – 126 MHz – CDCl}_3$

$\text{P}$

$\text{O}$

$\text{O}$

$\text{N}$
» $^1$H NMR – 360 MHz – CDCl₃

$^1$H NMR spectrum showing peaks at various ppm values.

» $^{13}$C NMR – 91 MHz – CDCl₃

$^{13}$C NMR spectrum showing peaks at various ppm values.
» **$^1$H NMR – 360 MHz – CDCl$_3$**

![$^1$H NMR spectrum]

17d

» **$^{13}$C NMR – 91 MHz – CDCl$_3$**

![$^{13}$C NMR spectrum]
H NMR – 400 MHz – CDCl₃

13C NMR – 101 MHz – CDCl₃
**$^1$H NMR – 360 MHz – CDCl$_3$**

![NMR Spectrum]

**$^{13}$C NMR – 91 MHz – CDCl$_3$**

![C NMR Spectrum]